

AMENDMENTS TO THE CLAIMS:

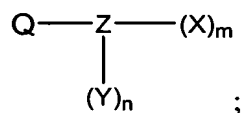
Claims 3, 4, 7-9, 11-14, 16, 19-21, 23, 24, 26-33, 35-37, 39-42, 45, 48-54, 57-62, 64, 65, 69-74, 76, 80, 83-94, 98, 100, 103-105, 108, 109, 111-115, 117, 119, 121-126, 129, 135, 136, 138, 141, 142, 148, 149, 154, 162 and 165 are cancelled herein without prejudice or disclaimer. Claims 1, 2, 5, 15, 17, 18, 22, 34, 43, 44, 47, 55, 63, 67, 68, 75, 77-79, 81, 82, 107, 110, 116, 120, 127, 128, 131-134, 137, 143, 144, 150-153, 155-157, 159, 160, 161, 163, 167 and 168 are amended herein. New claims 169-173 are added herein. This listing of claims will replace all prior versions, and listings of claims, in the application.

LISTING OF CLAIMS:

1. (Currently amended) A method of ~~identifying drug non-target biomolecules in a mixture of biomolecules~~, comprising:

(a) contacting a capture compound with a sample comprising interacting mixture of biomolecules with a collection of capture compounds, to effect capture of biomolecules in the sample, wherein:

~~the collection comprises a plurality of capture compounds, comprising sets of capture compounds,~~ compound has the formula:



~~wherein each set of capture compounds includes a moiety~~

X ~~that~~ is selected to covalently bind to biomolecules or to bind with sufficiently high affinity so that the resulting complexes of biomolecule/capture compounds are stable under conditions of mass spectrometric analysis; ~~a moiety~~

Y ~~that~~ is a pharmaceutical drug, drug fragment, drug intermediate, drug metabolite or prodrug selected to increase ~~increases~~ the selectivity of the binding by X such that the capture compound binds to fewer ~~biomolecules~~ biomolecules when the selectivity moiety Y is present than in its absence; ~~and a moiety~~

Q is a sorting function;

Z is a moiety for presenting X and Y;

m is an integer from 1 to 100; and

n is an integer from 1 to 100; and

(b) isolating and identifying ~~analyzing~~ the captured biomolecules ~~to identify drug non-~~
~~targets.~~

2. (Currently amended) ~~A~~ The method of identifying drug non-target biomolecules
in a mixture of biomolecules of claim 1, comprising:

~~——interacting mixture of biomolecules with a capture compound, wherein the capture~~
~~compound includes a moiety X that is selected to covalently bind to biomolecules or to bind with~~
~~sufficiently high affinity so that the resulting complexes of biomolecule/capture compounds are~~
~~stable under conditions of mass spectrometric analysis; a moiety Y that increases the selectivity~~
~~of the binding by X such that the capture compound binds to fewer biomolecules when the~~
~~selectivity moiety is present than in its absence; and a moiety Z for presenting X and Y; and~~
~~——analyzing wherein the captured biomolecules comprise drug targets and non-targets,~~
whereby to identify drug non-targets are identified.

Claims 3-4 (Cancelled).

5. (Currently amended) The method of claim 1 wherein, the moiety Y is linked to
the moiety Z in different orientations via different points of attachments on the Y moiety.

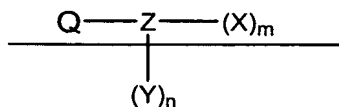
6. (Original) The method of claim 1, wherein the biomolecules are proteins.

Claims 7-9 (Cancelled).

10. (Original) The method of claim 1, wherein Q permits separation of capture
compounds by arraying of the capture compounds on a solid support by binding to the surface or
a molecule thereon.

Claims 11-14 (Cancelled).

15. (Currently amended) The method of claim 1, ~~wherein:~~ wherein
~~component capture compounds are selected from the group consisting of compounds that have~~
~~the formula(e):~~



~~Q-Z-(X)_m and Q-Z-(Y)_n;~~

Z is a moiety that is cleavable prior to or during mass spectrometric analysis of
biomolecules bound to the capture compound. [[;]]

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Preliminary Amendment

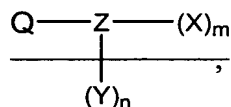
~~m is an integer that is 1 to 100; and~~

~~n is an integer from 1 to 100.~~

Claim 16 (Cancelled).

17. (Currently amended) The method of claim 1, ~~wherein:~~ wherein

~~the capture compounds are selected from the group consisting of compounds that have the formula(e):~~



~~Q-Z-(X)_m and Q-Z-(Y)_n;~~

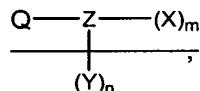
Z is a moiety that is not cleavable prior to or during mass spectrometric analysis of biomolecules bound to the capture compound. [[;]]

~~m is an integer that is 1 to 100; and~~

~~n is an integer from 1 to 100.~~

18. (Currently amended) The method of claim 17 1, wherein:

~~component capture compounds are selected from the group consisting of compounds that have the formula(e):~~



~~Q-Z-(X)_m and Q-Z-(Y)_n;~~

~~m is an integer that is 1 to 100;~~

~~n is an integer from 1 to 100; and~~

Q is a oligonucleotide or oligonucleotide analog that includes a single-stranded portion of sufficient length "j" to form a stable hybrid with a base-complementary single stranded nucleic acid molecule or analog.

Claims 19-21 (Cancelled).

22. (Currently amended) The method of claim 3 1, wherein Q has the formula $N^1_s B_i N^2_u$, wherein:

N^1 , B and N^2 are oligonucleotides or oligonucleotide analogs comprising s, t and u members, respectively;

B is a region of sequence permutations that contains at least two bases; and

sum of s, i and u is at least 5.

Claims 23 and 24 (Cancelled).

25. (Original) The method of claim 1, wherein Z is a photocleavable, acid cleavable, alkaline cleavable, oxidatively cleavable, or reductively cleavable group.

Claims 26-33 (Cancelled).

34. (Currently amended) The method of claim 1, wherein Z has the formula:
(S¹)_tM(R¹⁵)_a(S²)_bL, wherein:

S¹ and S² are spacer moieties;

t and b are each independently 0 or 1;

a is an integer from 0 to 4;

M is a central moiety possessing three or more points of attachment;

each R¹⁵ is a monovalent group independently selected from Y²R¹⁸;

each Y² is a divalent group independently having any combination of the following groups: a direct link, arylene, heteroarylene, cycloalkylene, >C(R¹⁷)₂, C(R¹⁷)=C(R¹⁷), >C=C(R²³)(R²⁴), >C(R²³)(R²⁴), C≡C, O, >S(A)_u, >P(D)_v(R¹⁷), >P(D)_v(ER¹⁷), >N(R¹⁷), >N(COR¹⁷), >N⁺(R²³)(R²⁴), >Si(R¹⁷)₂ and >C(E); where u is 0, 1 or 2; v is 0, 1, 2 or 3; A is O or NR¹⁷; D is S or O; and E is S, O or NR¹⁷; ~~that groups can be combined in any order;~~

R¹⁷ and R¹⁸ are each independently selected from the group consisting of hydrogen, halo, pseudohalo, cyano, azido, nitro, SiR²⁷R²⁸R²⁵, alkyl, alkenyl, alkynyl, haloalkyl, haloalkoxy, aryl, aralkyl, aralkenyl, aralkynyl, heteroaryl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, hydroxy, alkoxy, aryloxy, aralkoxy, heteroaralkoxy and NR¹⁹R²⁰;

R¹⁹ and R²⁰ are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl and heterocyclyl;

R²³ and R²⁴ are selected from (i) or (ii) as follows:

(i) R²³ and R²⁴ are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl and heteroaryl; or

(ii) R²³ and R²⁴ together form alkylene, alkenylene or cycloalkylene;

R²⁵, R²⁷ and R²⁸ are each independently a monovalent group selected from hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, haloalkoxy, aryl, aralkyl, aralkenyl, aralkynyl, heteroaryl,

heteroaralkyl, heteroaralkenyl, heteroaralkynyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, hydroxy, alkoxy, aryloxy, aralkoxy, heteroaralkoxy and $\text{NR}^{19}\text{R}^{20}$;

R^{15} , R^{17} , R^{18} , R^{19} , R^{20} , R^{23} , R^{24} , R^{25} , R^{27} and R^{28} can be substituted with one or more substituents each independently selected from Z^2 ; Z^2 is selected from alkyl, alkenyl, alkynyl, aryl, cycloalkyl, cycloalkenyl, hydroxy, $\text{S}(\text{O})_h\text{R}^{35}$; h is 0, 1 or 2, $\text{NR}^{35}\text{R}^{36}$, COOR^{35} , COR^{35} , $\text{CONR}^{35}\text{R}^{36}$, $\text{OC}(\text{O})\text{NR}^{35}\text{R}^{36}$, $\text{N}(\text{R}^{35})\text{C}(\text{O})\text{R}^{36}$, alkoxy, aryloxy, heteroaryl, heterocyclyl, heteroaryloxy, heterocycliloxy, aralkyl, aralkenyl, aralkynyl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, aralkoxy, heteroaralkoxy, alkoxycarbonyl, carbamoyl, thiocarbamoyl, alkoxycarbonyl, carboxyaryl, halo, pseudohalo, haloalkyl and carboxamido;

R^{35} and R^{36} are each independently selected from among hydrogen, halo, pseudohalo, cyano, azido, nitro, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkyl, alkenyl, alkynyl, haloalkyl, haloalkoxy, aryl, aralkyl, aralkenyl, aralkynyl, heteroaryl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, hydroxy, alkoxy, aryloxy, aralkoxy, heteroaralkoxy, amino, amido, alkylamino, dialkylamino, alkylarylamino, diarylamino and arylamino; and

L is a group that is cleavable prior to or during mass spectrometric analysis of the compound.

Claims 35-37 (Cancelled).

38. (Original) The method of claim 34, wherein L is a disulfide moiety, a photocleavable group, an acid cleavable group, an alkaline cleavable group, a oxidatively cleavable group, or a reductively cleavable group.

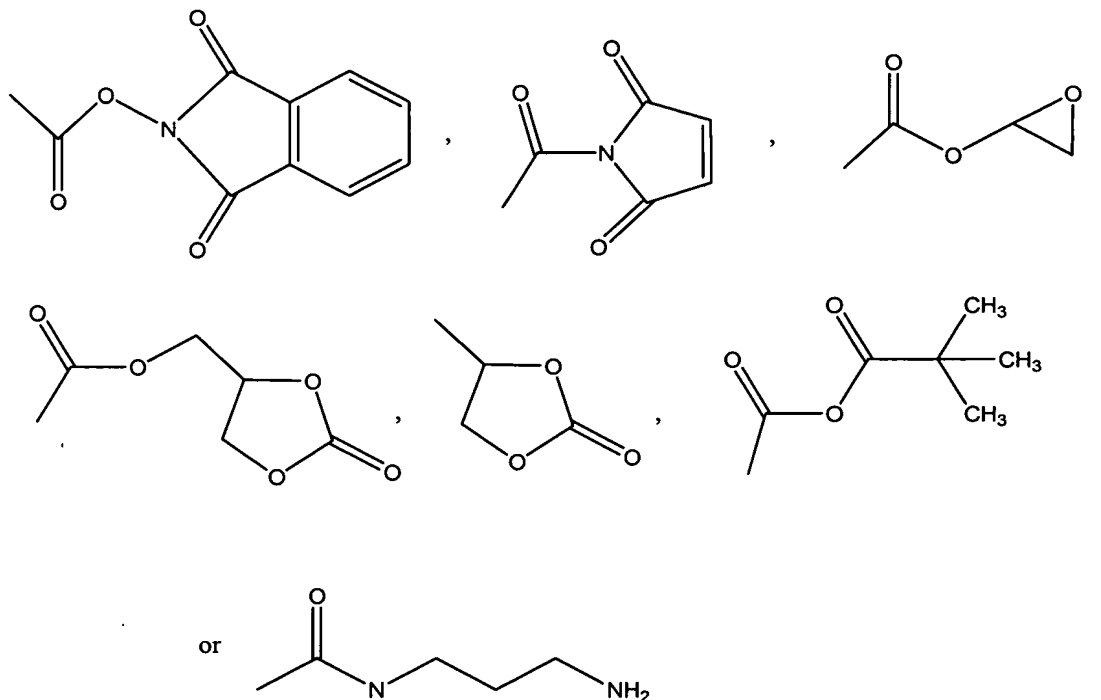
Claims 39-42 (Cancelled).

43. (Currently amended) The method of claim 1, wherein each X is selected from the group consisting of an active ester, an active halo moiety, an amino acid side chain-specific functional group, ~~a reagent that binds to active site of an enzyme, a ligand that binds to a receptor, and~~ a specific peptide that binds to a biomolecule surfaces, ~~a lectin, an antibody, an antigen, biotin, streptavidin.~~

44. (Currently amended) The method of claim 1, wherein an X is an α -halo ether, an α -halo carbonyl group, maleimido, a metal complex, an epoxide, and an isothiocyanate, ~~or an antibody against phosphorylated or glycosylated peptides/proteins.~~

Claim 45 (Cancelled).

46. (Original) The method of claim 1, wherein X is



47. (Currently amended) The method of claim 1, wherein ~~member~~ the capture compounds comprise a mass modifying tag linked to Z.

Claims 48-54 (Cancelled).

55. (Currently amended) The method of claim 3 18, wherein ~~a composition,~~ comprising the collection of capture compounds is are hybridized to a plurality of oligonucleotides or analogs thereof that comprise oligonucleotides that are complementary to each ~~each~~ Q.

56. (Original) The method of claim 55, wherein the oligonucleotides or analog thereof that are complementary to Q are immobilized on a solid support as an array.

Claims 57-62 (Cancelled).

63. (Currently amended)) The method of claim 3 1, wherein the Z moiety of the capture compound ~~compounds in the collection comprises Z, which~~ comprises a ~~reagent of a~~ functionality conferring luminescence, fluorescence, chemiluminescence or assay or a group that is detected in a colorimetric ~~properties. assay; and a sorting group Q that comprises a single-stranded oligonucleotide.~~

Claims 64 and 65 (Cancelled).

66. (Original) The method of claim 1, wherein the capture compounds further comprise a solubility group W that influences the solubility properties of the capture compound.

67. (Currently amended) The method of claim 1, wherein the selectivity function Y is a drug or drug intermediate/fragment is selected from among those set forth in Figure 17 and Figure 21 ~~and/or the reactivity function X is selected from those set forth in Figure 16.~~

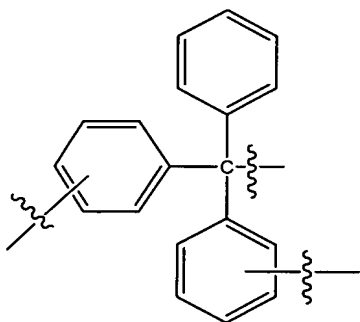
68. (Currently amended) The method of claim 1, wherein the ~~selectivity function Y is selected from those set forth in Figure 21 and/or the~~ reactivity function X is selected from those set forth in Figure 16.

Claims 69-74 (Cancelled).

75. (Currently amended) The method of claim 3 1, wherein Q is biotin.

Claim 76 (Cancelled).

77. (Currently amended) The method of claim ~~76~~ 1, wherein Z has the formula:



78. (Currently amended) The method of claim ~~76~~ 132, wherein X is selected from the groups set forth in Figure 16.

79. (Currently amended) The method of claim ~~76~~ 132, wherein Y is selected from the groups set forth in Figure 17.

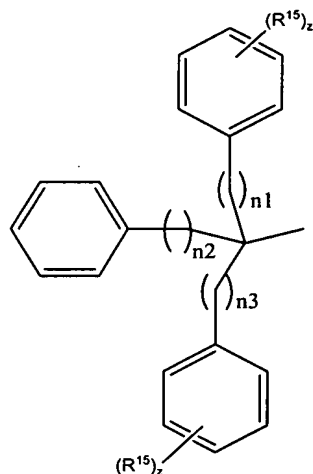
Claim 80 (Cancelled).

81. (Currently amended) A collection of capture compounds, comprising a plurality of capture compounds, ~~comprising sets of capture compounds~~, wherein each set of capture compounds includes:

a moiety X that is selected to covalently bind to biomolecules or to bind with sufficiently high affinity so that the resulting complexes of biomolecule/capture compounds are stable under conditions of mass spectrometric analysis;

a moiety Y that increases the selectivity of the binding by X such that the capture compound binds to fewer ~~biomolecules~~ biomolecules when the selectivity moiety is present than in its absence; and

a moiety Z for presenting X and Y, wherein the moiety Z is



wherein R^{15} ~~as described above~~ is H, OH, OR^{51} , SH, SR^{51} , NH_2 , NHR^{51} , $N(R^{51})_2$, F, Cl, Br, I, SO_3H , PO_4 , CH_3 , CH_2CH_3 , $CH(CH_3)_2$ or $C(CH_3)_3$; where R^{51} is straight or branched chain alkyl, straight or branched chain alkenyl, straight or branched chain alkynyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, straight or branched chain aralkyl, straight or branched chain aralkenyl, straight or branched chain aralkynyl, straight or branched chain heteroaralkyl, straight or branched chain heteroaralkenyl, straight or branched chain heteroaralkynyl, straight or branched chain cycloalkylalkyl, straight or branched chain cycloalkylalkenyl, straight or branched chain cycloalkylalkynyl, straight or branched chain heterocyclylalkyl, straight or branched chain heterocyclylalkenyl or straight or branched chain heterocyclylalkynyl;

z is an integer from 1 to 4; and

n1, n2, n3 are 0 to 4 with the proviso that all n1, n2 and n3 are not equal to 0 at the same time.

82. (Currently amended) A capture compound selected from ~~figure 23~~ Figure 23A-23D.

Claims 83-94 (Cancelled).

95. (Original) A method for separating protein conformers, comprising:
contacting a composition comprising a biomolecule with a collection of capture
compounds of claim 81,
separating the members of the collection; and
identifying the bound proteins from the mixture, whereby each conformer has different
binding specificity for members of the collection. [new claim 43]

96. (Original) The method of claim 95, wherein identification is effected by mass
spectrometry.

97. (Original) The method of claim 95, wherein at least one conformer is associated
with a disease.

Claim 98 (Cancelled).

99. (Original) A method for identification of phenotype-specific biomolecules,
comprising:
sorting cells from a single subject according to a predetermined phenotype to
produce at least two separated sets of cells;
contacting mixtures of biomolecules from each set of sorted cells with a collection
of capture compounds of claim 81; and
comparing the patterns of biomolecules binding from each set to identify
biomolecules that differ for each set, thereby identifying phenotype-specific biomolecules.

Claim 100 (Cancelled).

101. (Original) The method of claim 99, wherein the biomolecules comprise proteins.

102. (Original) The method of claim 99, wherein the bound biomolecules are
identified by mass spectrometry.

Claims 103-105 (Cancelled).

106. (Original) The method of claim 99, wherein the phenotypes are diseased and
healthy phenotypes.

107. (Currently amended) The method of claim 106, wherein the ~~cells are~~ disease phenotype is a tumor and the healthy phenotype is non-tumor.

Claims 108 and 109 (Cancelled).

110. (Currently amended) The method of claim ~~83~~ 1, ~~further comprising wherein identification or detection~~ identifying or detecting a captured biomolecule ~~is effected~~ by mass spectrometric analysis ~~of the biomolecule-capture compound complexes.~~

Claims 111-115 (Cancelled).

116. (Currently amended) The method of claim ~~83~~ 1, wherein the ~~composition comprising a biomolecule is~~ sample comprises a biological sample, a body tissue or fluid or a cell lysate.

Claim 117 (Cancelled).

118. (Original) A system for analysis of mixtures of biomolecules, comprising:
a collection of capture compounds of claim 81;
a computer programmed with instructions for controlling and directing analysis of biomolecules using the collections;
a mass spectrometer; and
software for analysis of data produced by the mass spectrometer.

Claim 119 (Cancelled).

120. (Currently amended) The system of claim ~~113~~ 118, further comprising a liquid chromatographic device.

Claims 121-126 (Cancelled).

127. (Currently amended) A method for analyzing biomolecule interactions, comprising:

a) contacting a mixture of biomolecules with a collection of capture compounds of claim 81, to form a capture compound-biomolecule complexes, wherein:

the central core is not cleavable prior to or during mass spectrometric analysis of biomolecules bound to the capture compound; and

the complexes are stable to matrix assisted laser desorption ionization-time of flight (MALDI-TOF) mass spectrometry conditions;

b) contacting the capture compound-biomolecule complexes with a mixture containing compounds selected from the group consisting of mixtures of biomolecules and small molecules test compounds, wherein compounds in the mixture bind to biomolecules in the complexes;

c) before or after step b) immobilizing the capture compounds on a solid support via the sorting group of each set of capture compounds; and

d) analyzing the bound compounds by mass spectrometry.

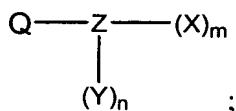
128. (Currently amended) The method of claim 127, wherein the small molecule test compounds are ~~candidates~~ candidate drugs and are selected from the group consisting of small organic molecules, peptides, peptide mimetics, antisense molecules or dsRNA, antibodies, fragments of antibodies and recombinant or synthetic antibodies and fragments thereof; and the method is a method for identifying candidate drugs that bind to biomolecules.

Claim 129 (Cancelled).

130. (Original) The method of claim 127, wherein the biomolecules are proteins.

131. (Currently amended) A method of analysis of biomolecules, comprising:

a) contacting a composition comprising a biomolecule with a collection ~~plurality of~~ capture compounds, ~~comprising sets of capture compounds~~, wherein ~~each set of the~~ capture compounds have the formula:



wherein:

~~includes a moiety X that~~ is selected to covalently bind to biomolecules or to bind with sufficiently high affinity so that the resulting complexes of biomolecule/capture compounds are stable under conditions of mass spectrometric analysis; ~~a moiety~~

Y is a moiety that increases the selectivity of the binding by X such that the capture compound binds to fewer biomolecules when the selectivity moiety is present than in its absence; ~~a moiety Q, such that each set contains a different Q, wherein~~

Q is a sorting function; ~~permits separation of each set and a moiety~~

Z is a moiety for presenting X, Y and Q;

m is an integer from 1 to 100; and

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n is an integer from 1 to 100;

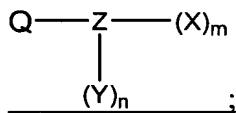
- b) digesting the captured biomolecules by chemical or enzymatic treatment;
- c) separating ~~each set of captured~~ the capture compounds based on the sorting moiety Q;

and

- d) analyzing ~~each set of~~ the capture compounds to identify the biomolecules.

132. (Currently amended) A method of analysis of biomolecules, comprising:

- a) contacting a composition comprising a biomolecule with a collection of capture compounds, wherein each capture compound ~~comprises~~ has the formula:



wherein:

~~a moiety X that~~ is selected to covalently bind to biomolecules or to bind with sufficiently high affinity so that the resulting complexes of biomolecule/capture compounds are stable under conditions of mass spectrometric analysis;

~~a moiety Y is a moiety~~ that increases the selectivity of the binding by X such that the capture compound binds to fewer ~~biomolecules~~ biomolecules when the selectivity moiety is present than in its absence; ~~a moiety Q, wherein~~

Q is a moiety that permits sorting; and ~~a moiety~~

Z is a moiety for presenting X, Y and Q;

- b) separating ~~each set of captured~~ capture compounds based on the sorting moiety Q;
- c) digesting the captured biomolecules by chemical or enzymatic treatment; and
- d) analyzing ~~each set of~~ the capture compounds to identify the biomolecules.

133. (Currently amended) The method of claim ~~83~~ 132, wherein the capture compounds are analyzed by mass spectrometry.

~~wherein:~~

~~the capture compounds comprise a sorting function for arraying the compounds on a solid support; and~~

~~the method further comprises arraying the capture compounds on a solid support before, during or after the contacting step, wherein:~~

~~the resulting biomolecule-capture compound complexes are at discrete spots on a solid support.~~

134. (Currently amended) The method of claim 133, wherein the mass spectrometric analysis ~~of the bound biomolecules~~, comprises:

(i) addition of matrix to the ~~biomolecule-capture agent complexes~~; capture compounds; and

~~(vi ii) spot-by-spot~~ matrix assisted laser desorption ionization-time of flight (MALDI-TOF) mass spectrometry.

Claims 135-136 (Cancelled).

137. (Currently amended) The method of claim 1, wherein Z has the formula:
 $(S^1)_t M(R^{15})_a (S^2)_b$, wherein:

S^1 and S^2 are spacer moieties;

t and b are each independently 0 or 1;

a is an integer from 0 to 4;

M is a central moiety possessing three or more points of attachment;

~~each~~ R^{15} is a monovalent group independently selected from $Y^2 R^{18}$;

~~each~~ Y^2 is a divalent group independently having any combination of the following groups: a direct link, arylene, heteroarylene, cycloalkylene, $>C(R^{17})_2$, $C(R^{17})=C(R^{17})$, $>C=C(R^{23})(R^{24})$, $>C(R^{23})(R^{24})$, $C\equiv C$, O, $>S(A)_u$, $>P(D)_v(R^{17})$, $>P(D)_v(ER^{17})$, $>N(R^{17})$, $>N(COR^{17})$, $>N^+(R^{23})(R^{24})$, $>Si(R^{17})_2$ and $>C(E)$; ~~where~~ wherein:

u is 0, 1 or 2;

v is 0, 1, 2 or 3;

A is O or NR^{17} ;

D is S or O; and

E is S, O or NR^{17} ; ~~that groups can be combined in any order;~~

R^{17} and R^{18} are each independently selected from the group consisting of hydrogen, halo, pseudohalo, cyano, azido, nitro, $SiR^{27}R^{28}R^{25}$, alkyl, alkenyl, alkynyl, haloalkyl, haloalkoxy, aryl, aralkyl, aralkenyl, aralkynyl, heteroaryl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl,

heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, hydroxy, alkoxy, aryloxy, aralkoxy, heteroaralkoxy and $\text{NR}^{19}\text{R}^{20}$;

R^{19} and R^{20} are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl and heterocyclyl;

R^{23} and R^{24} are selected from (i) or (ii) as follows:

(i) R^{23} and R^{24} are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl and heteroaryl; or

(ii) R^{23} and R^{24} together form alkylene, alkenylene or cycloalkylene;

R^{25} , R^{27} and R^{28} are each independently a monovalent group selected from hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, haloalkoxy, aryl, aralkyl, aralkenyl, aralkynyl, heteroaryl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, hydroxy, alkoxy, aryloxy, aralkoxy, heteroaralkoxy and $\text{NR}^{19}\text{R}^{20}$;

R^{15} , R^{17} , R^{18} , R^{19} , R^{20} , R^{23} , R^{24} , R^{25} , R^{27} and R^{28} can be substituted with one or more substituents each independently selected from Z^2 ; Z^2 is selected from alkyl, alkenyl, alkynyl, aryl, cycloalkyl, cycloalkenyl, hydroxy, $\text{S}(\text{O})_h\text{R}^{35}$; h is 0, 1 or 2, $\text{NR}^{35}\text{R}^{36}$, COOR^{35} , COR^{35} , $\text{CONR}^{35}\text{R}^{36}$, $\text{OC}(\text{O})\text{NR}^{35}\text{R}^{36}$, $\text{N}(\text{R}^{35})\text{C}(\text{O})\text{R}^{36}$, alkoxy, aryloxy, heteroaryl, heterocyclyl, heteroaryloxy, heterocycliloxy, aralkyl, aralkenyl, aralkynyl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, aralkoxy, heteroaralkoxy, alkoxycarbonyl, carbamoyl, thiocarbamoyl, alkoxycarbonyl, carboxyaryl, halo, pseudohalo, haloalkyl and carboxamido; and

R^{35} and R^{36} are each independently selected from among hydrogen, halo, pseudohalo, cyano, azido, nitro, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkyl, alkenyl, alkynyl, haloalkyl, haloalkoxy, aryl, aralkyl, aralkenyl, aralkynyl, heteroaryl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, hydroxy, alkoxy, aryloxy, aralkoxy, heteroaralkoxy, amino, amido, alkylamino, dialkylamino, alkylaryl amino, diarylamino and arylamino.

Claim 138 (Cancelled).

139. (Original) The method of claim 1, wherein X is a photoactivatable group.

140. (Original) The method of claim 139, wherein the capture compound interacts with the biomolecule mixture prior to activation of the photoactivatable group.

Claims 141 and 142 (Cancelled).

143. (Currently amended) The A method of claim 1, further comprising [[:]]
~~contacting a capture compound that comprises a drug with a sample containing~~
~~biomolecules to effect capture of biomolecules in the sample;~~
~~isolating and identifying the captured biomolecules; and~~
re-designing the drug moiety Y to eliminate or alter its binding interactions with a
captured biomolecule.

144. (Currently amended) The method of claim 143 1, further comprising identifying
a function of a captured biomolecule.

145. (Original) The method of claim 143, wherein the alteration in binding is an
increase in binding.

146. (Original) The method of claim 143, wherein the alteration in binding is a
decrease in binding.

147. (Original) The method of claim 143, wherein the biomolecule for which binding
is altered is a non-target biomolecule.

Claims 148 and 149 (Cancelled).

150. (Currently amended) The method of claim 143 1, ~~wherein the capture compound~~
~~comprises a moiety X that is selected to covalently bind to biomolecules or to bind with~~
~~sufficiently high affinity so that the resulting complexes of biomolecule/capture compounds are~~
~~stable under conditions of mass spectrometric analysis; a moiety Y that increases the selectivity~~
~~of the binding by X such that the capture compound binds to fewer biomolecules when the~~
~~selectivity moiety is present than in its absence; a moiety Q, wherein Q permits sorting; and a~~
~~moiety Z for presenting X, Y and Q;~~

wherein X is a latent reactivity group requiring activation following contacting with the
biomolecules to allow for reaction with the biomolecules.

151. (Currently amended) The method of claim 143 1, wherein the sample is contacted
with a collection of capture compounds.

152. (Currently amended) The method of claim 143 1, wherein the X moiety of the
capture compound comprises an azide, diazirine or a group active ester group which, following
activation, reacts with the biomolecule.

153. (Currently amended) The method of claim 143, wherein the method is repeated with the re-designed ~~drug moiety~~ Y linked to a capture compound to effect further modification thereof.

Claim 154 (Cancelled).

155. (Currently amended) The method of claim 143, wherein the captured ~~proteins~~ biomolecule for which binding is altered is a ~~are~~ drug target ~~proteins~~ protein.

156. (Currently amended) The method of claim 143, wherein the ~~capture~~ captured ~~proteins are~~ biomolecule for which binding is altered is a non-drug target ~~proteins~~ protein.

157. (Currently amended) The method of claim ~~143~~ 6, wherein the contacting step is performed under conditions whereby the interactions of the ~~drug moiety~~ Y with proteins in the sample reaches equilibrium.

158. (Original) The method claim 157, wherein after equilibrium the mixture is treated to form a covalent bond between the capture agent and the proteins.

159. (Currently amended) The method of claim 158, wherein the treatment comprises a change in pH, ~~or activation of a capture compound, wherein the capture compound comprises an inert reactivity group prior to activation.~~

160. (Currently amended) The method of claim ~~143~~ 1, wherein ~~the~~ a concentration of capture compound is varied in a plurality of different reactions.

161. (Currently amended) The method of claim 160, wherein a dissolution constant (K_d) ~~K_d~~ value is determined.

Claim 162 (Cancelled).

163. (Currently amended) The method of claim ~~162~~ 110, wherein the mass spectrometry format is selected from among matrix assisted laser desorption ionization (MALDI), continuous or pulsed electrospray (ES) ionization, ionspray, thermospray, and massive cluster impact mass spectrometry.

164. (Original) The method of claim 163, wherein the detection format is linear time-of-flight (TOF), reflectron time-of-flight, single quadrupole, multiple quadrupole, single magnetic sector, multiple magnetic sector, Fourier transform, ion cyclotron resonance (ICR), or ion trap.

Claim 165 (Cancelled).

166. (Currently amended) The method of claim ~~165~~ 144, wherein the function of a the biomolecule is determined by sequence alignment, pharmacophores, homology models and protein motif correlation, liver microsomes metabolic pathways, cDNA-expressed enzymes, signal pathways and back-mapping to yeast pathways, simulations and protein/protein interaction of pull-out proteins, native polymorphisms, knock-out/knock-in, flow cytometry, therapeutic activity of the drug, or prospective genotyping and prospective phenotyping.

167. (Currently amended) The method of claim 143, wherein:
the moiety Y is a first drug; and
redesigning the first drug results in a second drug with fewer side-effects or an increased therapeutic index as compared to the first drug.

168. (Currently amended) The method of claim ~~143~~ 1, wherein the drug is selected from among troglitazone, rosiglitazone, pioglitazone, methotrexate, atorvastatin, celecoxib, refecoxib and cerivastatin.

169. (New) The method of claim 158, wherein the treatment comprises activation with light.

170. (New) The method of claim 6, wherein the contacting step is performed under conditions, whereby the interactions of the moiety Y of the capture compound with proteins in the sample are kinetically controlled.

171. (New) The method of claim 22, where B is a single stranded DNA or RNA and the number of sequence permutations is equal to 4^i , wherein i is about 2 to about 25.

172. (New) The method of claim 172, where i is about 3 to about 5, 6, 7 or 8.

173. (New) The method of claim 133, wherein the moiety Y is selected from among a receptor ligand, an enzyme substrate, an enzyme inhibitor, a co-factor, a transition state analog, and a peptide selected to increase the selectivity of the binding by X such that the capture compound binds to fewer biomolecules when the selectivity moiety Y is present than in its absence.